p-Methoxyphenacyl Esters as Photodeblockable Protecting Groups for Phosphates

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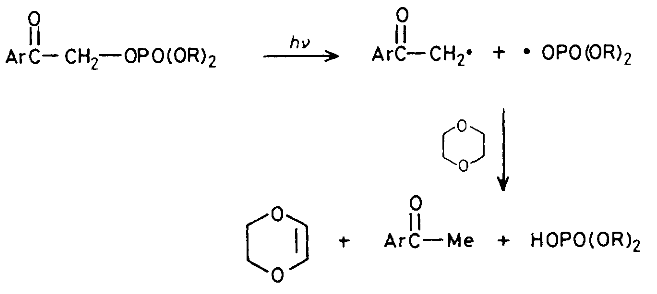
p-Methoxyphenacyl esters of substituted phosphates have been found to be photosensitive protecting groups which may be useful in biologically important phosphate synthesis.

Biological molecules containing variously substituted phosphate esters form a large part of the cellular matrix. Their importance is underlined by their presence in nucleic acids, proteins, coenzymes, carbohydrates, lipids, and steroids. The synthetic methodology for phosphorylation of these biologically important molecules in many cases requires the use of phosphate protecting groups which can be removed under mild, non-acidic, non-reductive conditions.[1] Although there are many phosphate protecting groups which can be deblocked by chemical or catalytic means,[2] photodeblocking is an attractive alternative owing to the potential experimental simplicity. Many of the available phototechniques[3] involve nitro-aromatic compounds which undergo photolytic side reactions involving the nitro groups and thus present purification problems.

We now report preliminary results on a new phosphate protecting group. Since the *p*-methoxyphenacyl group has been successfully used as a photosensitive group for carboxy groups,[4] its application to phosphates was indicated, particularly in view of Scaiano's[5] work on phosphate enhanced photofragmentation of aryl ketones. Model compounds were prepared in high yield (72% for R = Et; 89% for R = Ph)† by the reaction of α-diazo-*p*-methoxyacetophenone[6] with commercially available hydrogen phosphates [reaction (1)].



Scheme 1. Ar = *p*-MeOC$_6$H$_4$.

$$\mathrm{ArC(:O)CH_2N_2 + HOPO(OR)_2 \rightarrow ArC(:O)CH_2OPO(OR)_2 + N_2} \quad (1)$$

$$\mathrm{Ar} = p\text{-}\mathrm{MeOC_6H_4}$$

The results of the photodeblocking are in Table 1. Dioxane solutions (1—5 mM) were irradiated in a Pyrex photolysis cell under deoxygenated and dry N$_2$ in the presence of triethylamine (1 equiv.) at −20 °C for *ca.* 8 h with a 450 W medium-pressure mercury arc lamp. The solutions were evaporated and separated into neutral and acidic fractions. The neutral material was identified as *p*-methoxyacetophenone after chromatography. The diethyl phosphate was obtained as a syrupy liquid which was compared chromatographically and spectroscopically with authentic material, while diphenyl phosphate was a solid also characterized and compared with authentic material.

Table 1. Photolysis of *p*-methoxyphenacyl phosphates, *p*-MeOC$_6$H$_4$OPO(OR)$_2$.

R	M.p.,[a] *t*/°C	% Yield[b] *p*-MeOC$_6$H$_4$COMe	% Yield[b] (RO)$_2$PO$_2$H
Et	91—92	84	86
Ph	95—96	91	74[c]

[a] Of *p*-methoxyphenacyl phosphate. [b] Isolated yield. [c] M.p. 63—64 °C (M. Rapp, *Liebigs Ann. Chem.*, 1884, **224**, 158).

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† All new compounds were fully characterized spectroscopically and microanalytically.

The mechanism of the photoprocess, by analogy with *p*-methoxyphenacyl carboxylate ester cleavage, may be explained as a β-cleavage with dioxane acting as a hydrogen donor (Scheme 1).

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